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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,478	02/11/2005	Dodda Mohan Rao	S2096/20001	6950

3000 7590 11/08/2007

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EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	**PAPER NUMBER**
1626	

NOTIFICATION DATE	DELIVERY MODE
11/08/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,478	MOHAN RAO ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *2-23 and 25-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-17-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I in the reply filed on September 24, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 3-23 and 25-38 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on September 24, 2007.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on October 17, 2005 was filed in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 24 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims and nature of invention
Pharmaceutical composition comprising crystalline form III of linezolid.

The state of the prior art and level of predictability
It is well known that polymorphs convert to thermodynamically preferred forms unintentionally upon exposure to the energetics of pharmaceutical processing (Brittain et al., p. 332 1st paragraph, p. 334 1st paragraph), for example: production of bulk drug substance (Brittain et al., p. 333), particle size reduction (Brittain et al., p. 334), granulation (Brittain et al., p. 339). Furthermore, it is known in the art that the solid structure of a compound is lost when that compound is placed in solution (for example, see 1st paragraph 1, page 2 of http://www.expresspharmaonline.com/20031023/edit02.shtml). Therefore, the level of predictability is low in the art for preserving a particular crystalline form through the process of making a pharmaceutical composition. Absent a teaching of how the instantly claimed crystalline form can be maintained through the steps involved in pharmaceutical processing, one of ordinary skill would not know what precautions to take to avoid solid-to-solid (ie. crystal forms or amorphous) transformations during the formulation process.

The amount of direction and working examples provided
No working examples of the claimed pharmaceutical compositions are provided. No guidance is given for the method of making pharmaceutical compositions while maintaining the specifically claimed crystal form.

The quantity of experimentation needed to make or use the invention
Based on the lack of direction in the instant disclosure, in view of the low level of predictability in the art, one of ordinary skill is not enabled to make pharmaceutical compositions of any linezolid solid form. The quantity of experimentation to practice the claimed invention is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 and 2 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Barbachyn et al. (US 5,688,792 example 5 on columns 14 & 15).

Barbachyn et al. teach a solid form of linezolid which is obtained from a mixture of methanol and ethyl acetate. The reference does not teach a specific crystalline form of linezolid, because the inherent feature that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its

manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the disclosure of Barbachyn et al.

6. Claims 1 and 2 rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Meng (pg. 30, 1st paragraph).

Meng teaches a solid form of linezolid which is recrystallized from ethyl acetate and mineral ether. The reference does not teach a specific crystalline form of linezolid, because the inherent feature that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the disclosure of Meng.

7. Claims 1 and 2 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Pearlman et al. (WO 99/24393 example 8 on page 19).

Pearlman et al. teach a solid form of linezolid which is obtained from ethyl acetate. The reference does not teach a specific crystalline form of linezolid, because the inherent feature that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the disclosure of Pearlman et al.

8. Claims 1 and 2 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Perrault et al. (WO 02/085849 example 1 on page 14).

Perrault et al. teach a solid form of linezolid which is obtained from ethyl acetate using a procedure different from that reported by Pearlman et al. (WO 99/24393 example 8 on page 19). The reference does not teach a specific crystalline form of linezolid, because the inherent feature

that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics for which the reference happens to be silent. This is not an ordinary inherency situation, however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the disclosure of Perrault et al.

9. Claim 24 rejected under 35 U.S.C. 102(b) as being anticipated by Zyvox Consumer Information (published 11-16-2001).

The reference teaches pharmaceutical compositions of Zyvox (linezolid) in tablet, injection, and oral suspension. Further information on the composition of these formulations are provided by Zyvox's approved label.

The reference (Zyvox Consumer Information) does not teach a specific crystalline form of linezolid in the tablet formulaion, because the inherent feature that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art composition and the instantly claimed composition lies on characteristics for which the reference happens to be silent (ie. crystalline form of linezolid). This is not an ordinary inherency situation, however,

as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

Furthermore, it is noted that when a solid form is dissolved in an aqueous solution it no longer exists as the solid form. Rather, it adopts a "free form" which is the same as the one disclosed by the reference for the oral suspension and injection formulations.

10. Claim 24 rejected under 35 U.S.C. 102(a) as being anticipated by Pena et al. (WO 02/072066 pages 14-17).

The reference teaches pharmaceutical compositions of linezolid in carriers in which the drug is poorly soluble (see abstract). The reference does not teach a specific crystalline form of linezolid because the inherent feature that defines such form (eg. XRD data, IR data, etc.) is not disclosed. Thus, the difference between the prior art composition and the instantly claimed composition lies on characteristics for which the reference happens to be silent (ie. crystalline form of linezolid). This is not an ordinary inherency situation, however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). Furthermore, MPEP 2112.V states that "once a reference teaching product appearing to be substantially identical is

made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

To overcome this rejection, Applicant is requested to provide a showing of how the instantly claimed crystalline form is different from the disclosure of Pena et al.

Conclusion

11. No claims allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe
Art Unit 1626

REBECCA ANDERSON
PRIMARY EXAMINER